LINEAR POLYOL STABILIZED POLYFLUOROACRYLATE COMPOSITIONS

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a Non-Provisional Patent Application of U.S. Provisional Patent Application Ser. No. 61/165,899, filed Apr. 1, 2009, and U.S. Provisional Patent Application Ser. No. 61/091,097, filed Aug. 22, 2008, the entirety of which are herein incorporated by reference.

FIELD OF THE INVENTION

The present invention is directed to compositions of a stabilizing linear polyol and a salt of a crosslinked cation exchange polymer comprising a fluoro group and an acid group. These compositions are useful to bind potassium in the gastrointestinal tract.

BACKGROUND OF THE INVENTION

Potassium (K^+) is one of the most abundant intracellular cations. Potassium homeostasis is maintained predominantly through the regulation of renal excretion. Various medical conditions, such as decreased renal function, genitourinary disease, cancer, severe diabetes mellitus, congestive heart failure and/or the treatment of these conditions can lead to or predispose patients to hyperkalemia. Hyperkalemia can be treated with various cation exchange polymers including polyfluoroacrylic acid (polyFAA) as disclosed in WO 2005/097081.

Various polystyrene sulfonate cation exchange polymers (e.g., Kayexalate®, Argamate®, Kionex®) have been used to treat hyperkalemia in patients. These polymers and polymer compositions are known to have patient compliance issues, including dosing size and frequency, taste and/or texture, and gastric irritation. For example, in some patients, constipation develops, and sorbitol is thus commonly co-administered to avoid constipation, but this leads to diarrhea and other gastrointestinal side effects. It is also known that a wide variety of sugars can be used in pharmaceutical compositions. See, for example, EP 1785141.

Methods of reducing potassium and/or treatment of hyperkalemia have been found to raise patient compliance problems, in particular in chronic settings, which are solved by the present invention. Such problems include lack of tolerance of the therapeutically effective dose of polymeric binder (e.g., anorexia, nausea, gastric pain, vomiting and fecal impaction), dosing form (e.g., taste, mouth feel, etc.) and dose frequency (e.g., three times per day). The present invention solves these problems by providing a polymeric binder or a composition containing a polymeric binder that can be given once a day or twice a day without significant gastrointestinal side effects while retaining substantially similar efficacy. The methods of the present invention reduce the frequency and form of administration of potassium binder and increase tolerance, which will improve patient compliance, and potassium binding effectiveness.

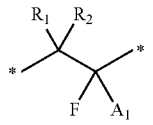
It has been found that linear polyols in particular have a stabilizing effect during storage on crosslinked poly alpha-fluoroacrylic acid in its salt form.

SUMMARY OF THE INVENTION

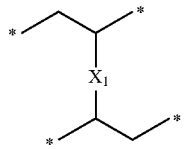
The present invention provides a pharmaceutical composition that comprises a salt of a crosslinked cation exchange polymer and a linear polyol stabilizer. Optionally, moisture is added to the composition. The salt of a preferred crosslinked cation exchange polymer is the product of the polymerization of at least two, and optionally three, different monomer units and is stabilized with respect to fluoride release. Among the various aspects of the invention is a composition comprising a linear polyol and a salt of a crosslinked cation exchange polymer comprising a fluoro group and an acid group that is the product of the polymerization of at least two, and optionally three, different monomer units. Typically, one monomer comprises a fluoro group and an acid group and the other monomer is a difunctional arylene monomer or a difunctional alkylene, ether- or amide-containing monomer, or a combination thereof.

A further aspect of the invention is a pharmaceutical composition comprising a crosslinked cation exchange polymer salt and from about 10 wt. % to about 40 wt. % of a linear polyol based on the total weight of the composition. The crosslinked cation exchange polymer comprises structural units corresponding to Formulae 1 and 2, Formulae 1 and 3, or Formulae 1, 2, and 3, wherein Formula 1, Formula 2, and Formula 3 are represented by the following structures:

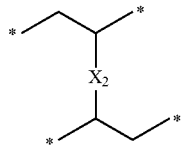
Formula 1



Formula 2

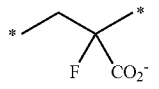


Formula 3



wherein R_1 and R_2 are each independently hydrogen, alkyl, cycloalkyl, or aryl; A_1 is carboxylic, phosphonic, or phosphoric; X_1 is arylene; and X_2 is alkylene, an ether moiety, or an amide moiety. In some instances, Formula 1, Formula 2, and Formula 3 are represented by the following structures:

Formula 1A



Formula 2A